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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/522,697 | 01/27/2005 | Joaquin Del Rio Zambrana | 4716CS-1 | 1882 |

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| EXAMINER | |
|---|---|
| NOLAN, JASON MICHAEL | |
| **ART UNIT** | **PAPER NUMBER** |
| 1626 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/522,697 | DEL RIO ZAMBRANA ET AL. | |
| | Examiner | Art Unit | |
| | Jason M. Nolan, Ph.D. | 1626 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6,9-18 and 22-25* is/are allowed.

6)☒ Claim(s) *7,8 and 19* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1-25** are pending in the instant application; of which, **Claims 1-8** are currently amended and **Claims 9-25** are new.

### *Response to Amendment*

Applicant's amendments, see Amendment – After Non-Final Rejection, filed 04/04/2007, with respect to the specification have been fully considered and are entered. Applicant's amendments to **Claims 1-8** have been fully considered and are entered. The objections to **Claims 1-2** are withdrawn; therefore, the compound, composition, and process **Claims 1-6, 9-18 & 21-25** are in condition for allowance. The 101 "use of" rejection to **Claims 7-8** is withdrawn per amendment; however, the 112-rejection to **Claims 7-8** and new method **Claim 19** is maintained and made FINAL.

### *Specification*

The disclosure is objected to because of the following informalities: Tables 1 & 2 are missing from the file, (*see* pages 20 & 21 of specification – blank pages). Appropriate correction is required.

### *Claim Rejections - 35 USC § 112, 1st Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 7, 8 & 19** are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for compounds and compositions and their use to provide neuroprotection against cerebral damage as well as the *treatment* of a pathological state, does not reasonably provide enablement for the *prophylaxis or prevention* of such conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'."

*In re Wands*, 8 USPQ2d 1400 (1988), discusses the following factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph:

1. ***The nature of the invention;***
2. ***The state of the prior art;***
3. ***The predictability or lack thereof in the art;***
4. ***The amount of direction or guidance present;***
5. ***The presence or absence of working examples;***
6. ***The breadth of the claims;***
7. ***The quantity of experimentation needed; and***
8. ***The level of skill in the art***

each of which is discussed in turn below.

***The nature of the invention***

The nature of the invention is compounds and compositions of Formula I, the process for preparing these compounds, and methods of using these compounds.

***The state of the prior art and the predictability or lack thereof in the art***

The state of the prior art, namely pharmacological art, involves screening *in vitro* and *in vivo* to determine if the compounds exhibit desired pharmacological activities, which are then tested for their efficacy on human beings. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. *In the instant case*, the claimed invention is highly unpredictable since one skilled in the art would recognize that a group of compounds and compositions may provide a treatment for a pathological state or cerebral damage, but it does not mean that the same group of compounds and compositions may prevent a pathological state or cerebral damage.

***The amount of direction or guidance present and the presence or absence of working examples***

There is no direction or guidance provided which supports Applicant's claimed method for the *prevention or prophylaxis* of a pathological state or cerebral damage, as indicated. The direction or guidance present in Applicants' Specification for a method of using the compounds and compositions of Formula I to *treat* clinical conditions of a

pathological state or cerebral damage can be found on pages 19-24, (*see* Examples 22-25).

***The breadth of the claims, quantity of experimentation, and level of skill in the art***

**Claims 7, 8 & 19** are drawn to the prophylaxis or treatment of a pathological state or cerebral damage. Prophylaxis is commonly known to be synonymous with prevention. In order to prevent a disease, one would need to precisely identify those subjects likely to acquire such a disease, administer Applicant's claimed invention, and then demonstrate that if the identified subject did not develop the disease, such an effect was the direct result of administration of the claimed invention.

Because of the aforementioned reasons, a person of skill in the art could not practice the claimed invention herein, or a person of skill in the art could practice the claimed invention herein only with undue experimentation and with no assurance of success. Deleting the words prevention and prophylaxis in **Claims 7, 8 & 19** can overcome this rejection.

***Claim Objections***

**Claim 20** is objected to as being dependent upon a rejected base Claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

The present invention pertains to the compounds of formula I in **Claim 1**, compositions thereof, the process of making said compounds, and methods of using these compounds for the treatment of a pathological state or cerebral damage. The compounds according to formula I are free of the prior art; nothing known in the art anticipates or renders the compounds of the instant application obvious.

The closest prior art related to the formula I is compound RN 65191-58-4, taught by Cheng, J.D. (*see* US Patent 4,055,410). Compound RN 65191-58-4 fulfills all of the limitations of formula I with the exception of $\mathbf{R_4}$, which is absent.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M$^{c}$Kane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner
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KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Joseph K. M$^{c}$Kane
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Date: July 6, 2007